Washington State Department of Health

ELABORATIONS

News and Issues for Washington's Clinical Laboratories

Volume IX Issue 5 June 2004

The Bioterrorism Corner: Ricin

by Candace Bunch
DOH, PHL Training Program

In 2003 letters laced with ricin were found addressed to the White House and the U.S. Department of Transportation. Then, in February 2004, ricin was found on an automated mail opening system in the Dirksen Senate Office Building. Though ricin, a poison derived from the castor bean, is deadly, large quantities would be required in order to turn it into a weapon that could harm large numbers of people. The U.S. Army Medical Research Institute of Infectious Disease in Fort Detrick, Maryland can test these ricin powders for their particle size and potency to determine how they were produced and who might have the means to do so. Ricin in particles smaller than five microns would be required in order to be an effective weapon via inhalation and this size is technologically difficult to produce.

Interestingly, castor beans and their toxicity have been known since ancient times. The name *Ricinus* is Latin for "tick" resulting from the markings on the bean and a bump at the end resembling a species of ticks. Egyptian tombs dating back to B.C. 4000 have held castor beans, and the Greeks were known to use castor seed oil for body anointments and lamps. For thousands of years castor seed oil was used as a laxative in India and as local medicine in China.

More recently, ricin was the main suspect in the 1978 assassination of Bulgarian exile Georgi Markov in London. It has been implicated in various other assassination attempts and conspiracies as well. Closer to home, ricin has become an object of obsession. In 1995, Thomas Lewis Lavy was arrested in Arkansas for possession of 130 grams of homemade ricin (while crossing the border into Canada). He claimed its use was necessary to kill the coyotes preying on his chickens. In July of 2003, a jury convicted Kenneth Olson, a software engineer and former Scoutmaster, of making and possessing powdered ricin. He was also accused of researching online how to create poisons that could kill without a trace. Traces of ricin were found around his workstation at Agilent Technologies, and three grams were found locked in a file cabinet.

Waste mash from the process of castor oil production contains 5% ricin by weight. Castor seed production worldwide is around 1 million tons per year and the

continued on page 2

Inside This Issue

Practice Guidelines

The following practice guidelines have been developed by the Clinical Laboratory Advisory Council. They can be accessed at the following website:
www.doh.wa.gov/lqa.htm

- Anemia
- ANA
- Bioterrorism Event Mgmt
- Bleeding Disorders
- Chlamydia
- Diabetes
- Group A Strep Pharyngitis
- Hepatitis
- HIV
- Infectious Diarrhea
- Intestinal Parasites
- Lipid Screening
- Point-of-Care Testing
- PSA
- Rash Illness
- Red Cell Transfusion
- Renal Disease
- STD
- Thyroid
- Tuberculosis
- Urinalysis
- Wellness

The Bioterrorism Corner: Ricin, continued from page 1

leading producing areas include India, China, Brazil and the former USSR.

Ricin toxin is quite stable and extremely toxic. Ricin cleaves one adenine residue near the 3' end of 28S RNA. This deletion then prevents an elongation factor to bind, and thus blocks protein synthesis. So, at the cellular level, ricin kills through inhibition of protein synthesis.

The clinical and pathological manifestations of ricin toxicity vary with the dose and the route of exposure. For example, inhalation of ricin results in respiratory distress and pulmonary lesions. Ingestion causes gastrointestinal hemorrhage with the necrosis of liver, spleen, and kidneys. Intramuscular intoxication causes severe localized pain, muscle and regional lymph node necrosis, and involvement of visceral organs. In addition, transient leukocytosis is often seen.

Due to terrorist activities and the availability of ricin, the push is on to find a vaccine that could be used tocombat ricin poisoning. Ellen Vitetta and colleagues at Southwestern Medical School have been working over twenty years to couple specific antibiodies to ricin's A chain in order to create an immunotoxin against lymphoma. Then they decided that perhaps by removing the active site they could use the molecule for vaccination purposes. They found it could immunize mice at 10 times its LD_{50} with no side effects.

Twinstrand Therapeutics, Cangene Corporation and the Defense R & D of Canada are developing antibodies for passive immunization. Recombinant ricin antigens provided by Twinstrand will be made using yeast expression. Cangene, with expertise in the preparation of hyperimmune products, will produce the hyperimmune ricin antisera in goats and ultimately develop human monoclonals to use against ricin.

Applying a ricin vaccine directly to the skin or via a patch is the current goal at Walter Reed Army Institute of Research. Researchers under Gary Matyas used a fragment of the ricin molecule as an antigen. In one set of studies, as a liquid, it was placed directly onto the skin of mice. In another set of studies they used patches impregnated with the molecule. All the mice with the direct application survived a lethal challenge of inhaled ricin. Those with patches had a survival rate of 70%.

For more information on how you can protect yourself from contamination through the mail, go to the Department of Homeland Security Information Bulletin: Guidance for Response to Ricin Delivered by Mail at http://www.dhs.gov/dhspublic/display?theme=34&content=3140&print=true.

ELABORATIONS is a free monthly publication of the Washington State Department of Health (DOH) Public Health Laboratories (PHL) and Office of Laboratory Quality Assurance (LQA).

Secretary, DOH: Mary Selecky
Health Officer: Maxine Hayes, MD, MPH
Director, PHL: Romesh Gautom, PhD
Program Manager, LQA: Gail Neuenschwander
Editor: Leonard Kargacin (206) 361-2804
Circulation: Leonard Kargacin (206) 361-2804

Comments, letters to the editor, information for publication, and requests for subscription can be directed to:
ELABORATIONS
Washington State Public Health Labs
1610 NE 150th Street
Shoreline, WA 98155

e-mail address: leonard.kargacin@doh.wa.gov

NOTE: Letters to the editor may be published unless specified otherwise by the author.

Website addresses:
DOH home page: http://www.doh.wa.gov
LQA home page: http://www.doh.wa.gov/lqa.htm
PHL home page:
http://www.doh.wa.gov/EHSPHL/PHL/default.htm

Bioterrorism Websites of Interest

The following websites are provided to offer additional information and educational opportunities regarding a variety of bioterrorism-related topics.

http://www.biomedtraining.org/

http://www.hsrnet.net/ahrq-ulp/bioterrorism/

http://www.homelanddefensejournal.com/

http://healthlinks.washington.edu/nwcphp/bttrain/phw/

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5041a2.htm

http://www.wmdfirstresponders.com/Biological.htm

http://www.loc.gov/rr/frd/pdf-files/Soc_Psych_of_Terrorism.pdf

Practice Guidelines

by Leonard Kargacin
DOH, Laboratory Quality Assurance

A critical area of concern in the current cost-conscious health care environment is optimization of service delivery. Over-utilization of laboratory testing can lead to needless and costly treatment for the patient. Under-utilization can result in a misdiagnosis and delays in treatment. To address inappropriate or unnecessary use of laboratory testing services, the Clinical Laboratory Advisory Council decided to establish a process for developing practice guidelines for clinical laboratory testing. The guidelines are for educational purposes only.

The intent of the guidelines is to help laboratorians answer questions they may get from clinicians on appropriate test ordering. The guidelines will also be useful to clinicians as a review of a typical test-ordering pattern for asymptomatic patients. The guidelines are a compilation of existing data, not original work by the Council. For the format, the Council elected to summarize existing information into simple, easy-to-use flow charts. Once a test has been identified by the Council as a candidate for a guideline, a Council workgroup is formed to develop a proposed guideline. The draft guideline is reviewed by the entire Council, members of the state's laboratory community and appropriate medical professional societies. Comments from the reviewers are evaluated by the Council workgroup and incorporated into the final document. The finalized guideline is disseminated to all clinical laboratories and other interested parties through this newsletter.

The final guidelines should be used strictly as educational guidelines. The individual clinician is in the best position to determine which tests are most appropriate for a particular patient.

Guidelines developed by the Council that have been previously published in E**LAB**ORATIONS include screening guidelines for anemia, ANA, bioterrorism event management, bleeding disorders, chlamydia, diabetes, group A strep pharyngitis, hepatitis, HIV, intestinal parasites, lipid, point-of-care testing, PSA, red cell transfusion, renal disease, STD, TB, thyroid, urinalysis microscopic and culture, and wellness screening. This issue of E**LAB**ORATIONS contains the guideline for evaluating rash illness.

11th Annual Clinical Laboratory Conference

by Leonard Kargacin
DOH, Laboratory Quality Assurance

The 11th Annual Clinical Laboratory Conference will be held on November 8, 2004 at the Seattle Marriott Hotel near Sea-Tac International Airport. This is an excellent opportunity to hear about the current status of health care from a variety of experts.

The program committee is in the process of finalizing the program. Dennis Weissman, President and Publisher of Washington G-2 Reports in Washington, D.C., will present the keynote address for the Conference. Meera Kanhouwa, MD, MHA, FACEP, Medical Director, Information Services at Swedish Medical Center in Seattle, has agreed to present an update on the Patient Safety Initiative. Mark Stern, MD, Medical Director of the Washington State Department of Corrections, will present information on Evidence-based Medicine. The committee is in the process of identifying a speaker to speak on reimbursement issues.

Plan to attend this year's conference. Program flyers and registration forms will be mailed out in August/September. In the meantime, mark your calendars for November 8.

Guideline for Evaluating Patients for Rash Illness

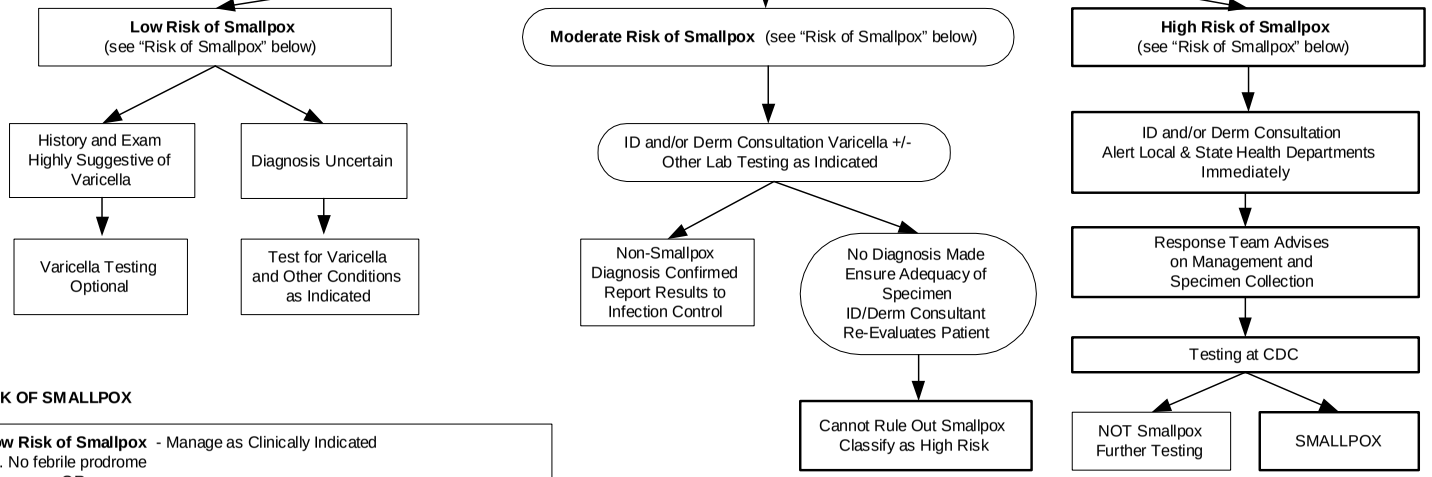
Washington State Clinical Laboratory Advisory Council (CLAC)
May 2004

Patient with Acute, Generalized Vesicular or Pustular Rash Illness

Institute Airborne & Contact Precautions Alert Infection Control on Admission

Telephone Numbers For your Facility

Laboratory Director_____
Laboratory Supervisor_____
Lead Technologist_____
Infection Control_____
Local Health Jurisdiction_____
Washington State DOH, Communicable Disease Epidemiology: (206) 361-2914 or 1 (800) 539-4344



RISK OF SMALLPOX

Low Risk of Smallpox - Manage as Clinically Indicated
1. No febrile prodrome
   OR
1. Febrile prodrome (see Major Smallpox Criteria) AND
2. Fewer than four Minor smallpox criteria (see Minor Smallpox Criteria)

Moderate Risk of Smallpox - Urgent Evaluation
1. Febrile prodrome (see Major Smallpox Criteria) AND
2. One other MAJOR smallpox criterion (see Major Smallpox Criteria)
   OR
1. Febrile prodrome (see Major Smallpox Criteria) AND
2. Four or more MINOR smallpox criteria (see Minor Smallpox Criteria)

High Risk of Smallpox - Report Immediately
1. Febrile prodrome (see Major Smallpox Criteria) AND
2. Classic smallpox lesion (see Major Smallpox Criteria) AND
3. Lesions in same stage of development (see Major Smallpox Criteria)

MAJOR SMALLPOX CRITERIA

FEBRILE PRODROME: occurring 1-4 days before rash onset: fever greater than or equal to 101ºF and at least one of the following: Prostration, headache, backache, chills, vomiting, or severe abdominal pain.

CLASSIC SMALLPOX LESIONS: deep-seated, firm/hard, round well-circumscribed vesicles or pustules; as they evolve, lesions may become umbilicated or confluent

LESIONS IN THE SAME STAGE OF DEVELOPMENT: on any one part of the body (e.g., the face, or arm) all lesions are in the same stage of development (i.e., all are vesicles, or all are pustules)

MINOR SMALLPOX CRITERIA

- Centrifugal distribution: greatest concentration of lesions on face and distal extremities
- First lesions on the oral mucosa/palate, face, or forearms
- Patient appears toxic or moribund
- Slow evolution: lesions evolve from macules to papules to pustules over days (each stage lasts 1-2 days)
- Lesions on the palms and soles

Differentiating Chickenpox From Smallpox

Chickenpox (varicella) is the most likely condition to be confused with Smallpox

In Chickenpox

- No or mild prodrome
- Lesions are superficial vesicles: "Dewdrop on a rose petal"
- Lesions appear in crops: on any one part of the body there are lesions in different stages (pustules, vesicles, crusts)
- Centripetal distribution: greatest concentration of lesions on the trunk, fewest lesions on distal extremities. May involve the face/scalp. Occasionally entire body equally affected.
- First lesions appear on the face or trunk
- Patients rarely toxic or moribund
- Rapid evolution: lesions evolve from macules; papules; vesicles; crusts quickly (<24 hours)
- Palms and soles rarely involved
- Patient lacks reliable history of varicella or varicella vaccination
- 50-80% recall an exposure to chickenpox or shingles 10-21 days before rash onset

Common Conditions That Might Be Confused With Smallpox

Condition	Clinical Clues
Varicella (Primary infection with varicella-zoster virus)	Most common in children <10 years; children usually do not have a viral prodrome
Disseminated herpes zoster	Immunocompromised or elderly persons; rash looks like varicella, usually begins in dermatomal distribution
Impetigo (*Streptococcus pyogenes*, *Staphylococcus aureus*)	Honey-colored crusted plaques with bullae are classic but may begin as vesicles; regional not disseminated rash; patients generally not ill
Drug eruptions	Exposure to medications; rash often generalized
Contact dermatitis	Itching; contact with possible allergens; rash often localized in pattern suggesting external contact
Erythema multiforme minor	Target, "bulls eye", or iris lesions; often follows recurrent herpes simplex virus infections; may involve hands and feet (including palms and soles)
Erythema multiforme (incl. Stevens Johnson Syndrome)	Major form involves mucous membranes and conjunctivae; may be target lesions or vesicles
Enteroviral infection esp. Hand, Foot and Mouth disease	Summer and fall; fever and mild pharyngitis 1-2 days before rash onset; lesions initially maculopapular but evolve into whitish-gray tender, flat often oval vesicles; peripheral distribution (hands, feet, mouth, or disseminated)
Disseminated herpes simplex	Lesions indistinguishable from varicella; immunocompromised host
Scabies; insect bites (incl. fleas)	Itching is a major symptom; patient is not febrile and is otherwise well
Molluscum cantagiosum	May disseminate in immunocompromised persons

Additional Smallpox Information

Laboratory Diagnostics: Clinical evaluation and a careful patient history of recent smallpox vaccination or contact with a recent vaccinee are the mainstays of diagnosis of smallpox vaccine-related adverse events. In situations where clinical diagnosis is not straightforward, laboratory diagnostics for vaccinia might be helpful and might prevent inappropriate use of potentially toxic therapies. However, diagnostics for conditions easily confused with vaccinia infection (i.e., varicella, herpes zoster, herpes simplex, and enteroviruses) should be considered first, in particular for a nonvaccinee or someone believed to be a noncontact of a vaccinee. Serologic testing for vaccinia is probably uninformative because it cannot be used to distinguish vaccinia immunity from vaccinia infection unless baseline antibody titers are available. Diagnostic tests for vaccinia include electron microscopy to identify presence of orthopoxvirus, and gene amplification (polymerase chain reaction [PCR]), and viral culture for vaccinia. Regarding vaccinia, these tests are available only for research purposes, but are undergoing multicenter validation studies that might enable FDA to approve the test reagents for diagnostic use. After that approval, testing will be made available through the Laboratory Response Network (LRN), an extensive system of public health and private laboratories that can be accessed through consultation with state and local health departments. Consultation regarding appropriate use of specialized vaccinia laboratory testing will be available through CDC.

Laboratory Specimen Collection: A suspected case of an adverse event after smallpox vaccination should be promptly reported to the appropriate local, state, or territorial health department. When appropriate, public health officials might recommend that clinical specimens be collected for further evaluation of a possible case.

Specimen Labeling and Handling: Label all tubes, vials, and microscope slide holders with patient's name, unique identifier, date of collection, source of specimen (vesicle, pustule, scab, or fluid), and name of person collecting the specimen.

Infection Control Procedures: Wear appropriate personal protective equipment. (Contact appropriate infection control personnel.)

Reference: Centers for Disease Control and Prevention Evaluating Patients for Smallpox, Version 1.0; January 31, 2002.

For more information, please go to the CDC website http://www.bt.cdc.gov/agent/smallpox/index.asp and http://www.bt.cdc.gov/EmContact/index.asp

TIPS for Proficiency Testing Success

Improve your chances for successful participation in PT by implementing the following suggestions:

Retain all raw data: Save data showing the workup of PT samples, instrument printouts, worksheets, log sheets.

Fill in the Method Code: Do not leave blank.

Correctly report the reason PT was not done: If you are unable to test for some reason, indicate this on the answer sheet. If you discontinued testing for an analyte, indicate this on the sheet. Immediately notify LQA of any change.

Be timely: Always be sure to meet the deadline for returning your results.

Review the individual test results, not just the event summary page: Review your graded PT results with your lab director. Document corrective action for scores below 80%. Evaluate all ungraded results.

Calendar of Events

PHL Training Classes:
(http://www.doh.wa.gov/EHSPHL/PHL/train.htm)

Basic Blood Cell Morphology
September 9 Shoreline

Handling & Shipping of Biohazadous Materials
September 22 Shoreline

Northwest Medical Laboratory Symposium
October 20-23 Portland

11th Annual Clinical Laboratory Conference
November 8 Seattle

2005 WSSCLS/NWSSAMT Spring Meeting
April 28-30, 2005 Spokane

Contact information for the events listed above can be found on page 2. The Calendar of Events is a list of upcoming conferences, deadlines, and other dates of interest to the clinical laboratory community. If you have events that you would like to have included, please mail them to ELABORATIONS at the address on page 2. Information must be received at at least one month before the scheduled event. The editor reserves the right to make final decisions on inclusion.

ELABORATIONS
Washington State Department of Health
1610 NE 150th Street
Shoreline, WA 98155